

AMENDMENTS TO THE CLAIMS:

Claim 12 has been cancelled. Claims 1, 7, 8, 15, 16, 17, 20, 26, 30, 33, 34, 35, 38, 44, 49, 52, and 53 have been amended. Claims 1, 7, 8, 12, 15-17, 19, 20, 26, 30, 33-35, 37, 38, 44, 49, 52, and 53 are pending. The following is the status of the claims of the above-captioned application, as amended.

1. (Currently Amended) A method of producing a heterologous ~~biological substance~~ ~~polypeptide~~, comprising:

(a) cultivating a mutant of a parent *Aspergillus niger* strain in a medium suitable for the production of the heterologous ~~biological substance~~ ~~polypeptide~~, wherein (i) the mutant strain comprises a first nucleotide sequence encoding the heterologous ~~biological substance~~ ~~polypeptide~~ and one or more second nucleotide sequences comprising a modification of *glaA*, and ~~at least one of the genes selected from the group consisting of~~ *asa*, *amyA*, *amyB*, *prtT*, and *oah*, and (ii) the mutant strain is deficient in the production of glucoamylase, ~~and at least one enzyme selected from the group consisting of~~ acid stable alpha-amylase, neutral alpha-amylase A, and neutral alpha-amylase B, protease, and oxalic acid hydrolase compared to the parent *Aspergillus niger* strain when cultivated under identical conditions; and

(b) recovering the heterologous ~~biological substance~~ ~~polypeptide~~ from the cultivation medium.

2. (Canceled).

3. (Canceled).

4. (Canceled).

5. (Canceled).

6. (Canceled).

7. (Currently Amended) The method of claim 1, wherein the ~~biological substance~~ ~~heterologous polypeptide~~ encoded by the first nucleotide sequence is a ~~biopolymer~~ an antibody, antigen, antimicrobial peptide, enzyme, growth factor, hormone, immunodilator,

neurotransmitter, receptor, reporter protein, structural protein, or transcription factor.

8. (Currently Amended) The method of claim 7, wherein the ~~biopolymer enzyme~~ is selected from the group consisting of a nucleic acid, polyamide, polyamine, polyol, polypeptide, and polysaccharide an oxidoreductase, transferase, hydrolase, lyase, isomerase, or ligase.

9. (Canceled).

10. (Canceled).

11. (Canceled).

12. (Cancelled).

13. (Canceled).

14. (Canceled).

15. (Currently Amended) The method of claim 1, wherein the mutant strain produces at least 25% less enzyme for each of glucoamylase, and one or more enzymes selected from the group consisting of acid stable alpha-amylase, neutral alpha-amylase A, and neutral alpha-amylase B, protease, and oxalic acid hydrolase compared to the parent *Aspergillus niger* strain when cultivated under identical conditions.

16. (Currently Amended) The method of claim 1, wherein the mutant strain is completely deficient in glucoamylase, ~~and at least one enzyme selected from the group consisting of acid stable alpha-amylase, neutral alpha-amylase A, and neutral alpha-amylase B, protease, and oxalic acid hydrolase~~ compared to the parent *Aspergillus niger* strain when cultivated under identical conditions.

17. (Currently Amended) The method of claim 1, wherein the mutant strain further comprises a modification of one or more genes which encode ~~a~~ an enzyme having proteolytic activity.

18. (Canceled).

19. (Original) The method of claim 1, wherein the mutant strain further comprises a modification of one or more genes encoding an enzyme selected from the group consisting of a carbohydrolase, carboxypeptidase, catalase, cellulase, chitinase, cutinase, cyclodextrin glycosyltransferase, deoxyribonuclease, esterase, galactosidase, beta-galactosidase, glucose oxidase, glucosidase, haloperoxidase, hemicellulase, invertase, isomerase, laccase, ligase, lipase, lyase, mannosidase, oxidase, pectinolytic enzyme, peroxidase, phytase, phenoloxidase, polyphenoloxidase, ribonuclease, transferase, alpha-1,6-transglucosidase, transglutaminase, and xylanase.

20. (Currently Amended) A mutant of a parent *Aspergillus niger* strain, comprising a first nucleotide sequence encoding a heterologous ~~biological substance~~ polypeptide and one or more second nucleotide sequences comprising a modification of *glaA₁*, ~~and at least one of the genes selected from the group consisting of~~ *asa*, *amyA*, *amyB*, *prtT*, and *oah*, wherein the mutant strain is deficient in glucoamylase, ~~and at least one enzyme selected from the group consisting of~~ acid stable alpha-amylase, neutral alpha-amylase A, and neutral alpha-amylase B, protease, and oxalic acid hydrolase compared to the parent *Aspergillus niger* strain when cultivated under identical conditions.

21. (Canceled).

22. (Canceled).

23. (Canceled).

24. (Canceled).

25. (Canceled)

26. (Currently Amended) The mutant strain of claim 20, wherein the ~~biological substance~~ heterologous polypeptide encoded by the first nucleotide sequence is ~~a biopolymer~~ an antibody, antigen, antimicrobial peptide, enzyme, growth factor, hormone, immunodilator, neurotransmitter, receptor, reporter protein, structural protein, or transcription factor.

27. (Canceled).
28. (Canceled).
29. (Canceled).
30. (Currently Amended) The mutant strain of claim 20 26, wherein the ~~biological substance enzyme encoded by the first nucleotide sequence is a metabolite an oxidoreductase, transferase, hydrolase, lyase, isomerase, or ligase.~~
31. (Canceled).
32. (Canceled).
33. (Currently Amended) The mutant strain of claim 20, which produces at least 25% less ~~enzyme for each of glucoamylase and one or more enzymes selected from the group consisting of acid stable alpha-amylase, neutral alpha-amylase A, and neutral alpha-amylase B, protease, and oxalic acid hydrolase compared to the parent *Aspergillus niger* strain when cultured under identical conditions.~~
34. (Currently Amended) The mutant strain of claim 20, which is completely deficient in glucoamylase ~~and one or more enzymes selected from the group consisting of acid stable alpha-amylase, neutral alpha-amylase A, and neutral alpha-amylase B, protease, and oxalic acid hydrolase compared to the parent *Aspergillus niger* strain when cultured under identical conditions.~~
35. (Currently Amended) The mutant strain of claim 20, which further comprises a modification of one or more genes which encode ~~a~~ an enzyme having proteolytic activity.
36. (Canceled).
37. (Original) The mutant strain of claim 20, which further comprises a modification of one or more genes encoding an enzyme selected from the group consisting of a carbohydrase, carboxypeptidase, catalase, cellulase, chitinase, cutinase, cyclodextrin glycosyltransferase,

deoxyribonuclease, esterase, galactosidase, beta-galactosidase, glucose oxidase, glucosidase, haloperoxidase, hemicellulase, invertase, isomerase, laccase, ligase, lipase, lyase, mannosidase, oxidase, pectinolytic enzyme, peroxidase, phytase, phenoloxidase, polyphenoloxidase, ribonuclease, transferase, alpha-1,6-transglucosidase, transglutaminase, and xylanase.

38. (Currently Amended) A method for obtaining a mutant of a parent *Aspergillus niger* strain, comprising:

(a) introducing into the parent *Aspergillus niger* strain a first nucleotide sequence encoding a heterologous ~~biological substance~~ polypeptide and one or more second nucleotide sequences comprising a modification of *glaA₁*, ~~and at least one of the genes selected from the group consisting of~~ *asa*, *amyA*, *amyB*, *prtT₁* and *oah*; and

(b) identifying the mutant strain from step (a) comprising the modified nucleotide sequence, wherein the mutant strain is deficient in the production of glucoamylase, ~~and at least one enzyme selected from the group consisting of~~ acid stable alpha-amylase, neutral alpha-amylase A, ~~and~~ neutral alpha-amylase B, protease, and oxalic acid hydrolase compared to the parent *Aspergillus niger* strain when cultivated under identical conditions.

39. (Canceled).

40. (Canceled).

41. (Canceled).

42. (Canceled).

43. (Canceled).

44. (Currently Amended) The method of claim 38, wherein the ~~biological substance~~ heterologous polypeptide encoded by the first nucleotide sequence is ~~a biopolymer~~ an antibody, antigen, antimicrobial peptide, enzyme, growth factor, hormone, immunodilator, neurotransmitter, receptor, reporter protein, structural protein, or transcription factor.

45. (Canceled).

46. (Canceled).
47. (Canceled).
48. (Canceled).
49. (Currently Amended) The method of claim 38 44, wherein the ~~biological substance enzyme needed by the first nucleotide sequence is a metabolite~~ an oxidoreductase, transferase, hydrolase, lyase, isomerase, or ligase.
50. (Canceled).
51. (Canceled).
52. (Currently Amended) The method of claim 38, wherein the mutant strain produces at least 25% less enzyme for each of glucoamylase, ~~and one or more enzymes selected from the group consisting of~~ acid stable alpha-amylase, neutral alpha-amylase A, ~~and~~ neutral alpha-amylase B, protease, and oxalic acid hydrolase compared to the parent *Aspergillus niger* strain when cultured under identical conditions.
53. (Currently Amended) The method of claim 38, wherein the mutant strain is completely deficient in glucoamylase, ~~and one or more enzymes selected from the group consisting of~~ acid stable alpha-amylase, neutral alpha-amylase A, ~~and~~ neutral alpha-amylase B, protease, and oxalic acid hydrolase compared to the parent *Aspergillus niger* strain when cultured under identical conditions.
54. (Canceled).
55. (Canceled).
56. (Canceled).